Amendments to the Specification:

Please replace the paragraph beginning at page 9, line 12, with the following:

--In all the figure legends, a peptide having an amino acid sequence of SALLRSIPA (SEQ ID NO:1) is referred to as "SAL," and a peptide having a sequence of NAPVSIPQ (SEQ ID NO:2) is referred to as "NAP."--

Please replace the paragraph beginning at page 9, line 17, with the following:

--The phrase "ADNF polypeptide" refers to one or more activity dependent neurotrophic factors (ADNF) that have an active core site comprising the amino acid sequence of SALLRSIPA (SEQ ID NO:1) (referred to as "SAL") or NAPVSIPQ (SEQ ID NO:2) (referred to as "NAP"), or conservatively modified variants thereof that have neurotrophic/neuroprotective activity as measured with *in vitro* cortical neuron culture assays described by, *e.g.*, Hill *et al.*, *Brain Res*. 603, 222-233 (1993); Venner & Gupta, *Nucleic Acid Res*. 18, 5309 (1990); and Peralta *et al.*, *Nucleic Acid Res*. 18, 7162 (1990); Brenneman *et al.*, *Nature* 335, 636 (1988); or Brenneman *et al.*, *Dev. Brain Res.* 51:63 (1990); Forsythe & Westbrook, *J. Physiol. Lond.* 396:515 (1988). An ADNF polypeptide can be an ADNF I polypeptide, an ADNF III polypeptide, their alleles, polymorphic variants, or interspecies homolog, or any subsequences thereof (*e.g.*, SALLRSIPA (SEQ ID NO:1) or NAPVSIPQ (SEQ ID NO:2)) that exhibit neuroprotective/neurotrophic action on, *e.g.*, neurons originating in the central nervous system either *in vitro* or *in vivo*. An "ADNF polypeptide" can also refer to a mixture of an ADNF I polypeptide and an ADNF III polypeptide.--

Please replace the paragraph beginning at page 21, line 18, with the following:

--Within the above formula for the ADNF I polypeptide, x and y are independently selected and are equal to zero or one. The term independently selected is used herein to indicate that x and y may be identical or different. For example, x and y may both be zero or, alternatively, x and y may both be one. In addition, x may be zero and y may be one or, alternatively, x may be one and y may be zero. Moreover, if x and y are both one, the amino acid sequences R^1 and R^2 may be the same or different. As such, the amino acid sequences R^1 and R^2 are independently selected. If R^1 and R^2 are the same, they are identical in terms of both chain length and amino acid composition. For example, both R^1 and R^2 may be Val-Leu-Gly-Gly-Gly (SEQ ID NO:5); see SEQ ID NO:14. If R^1 and R^2 are different, they can differ from one another in terms of chain length and/or amino acid composition and/or order of amino acids in the amino acids sequences. For example, R^1 may be Val-Leu-Gly-Gly-Gly (SEQ ID NO:5), whereas R^2 may be Val-Leu-Gly-Gly (SEQ ID NO:9); see SEQ ID NO:15. Alternatively, R^1 may be Val-Leu-Gly-Gly-Gly (SEQ ID NO:5), whereas R^2 may be Val-Leu-Gly-Gly-Val ~~(SEQ ID NO:13)~~ (SEQ ID NO:10); see SEQ ID NO:16. Alternatively, R^1 may be Val-Leu-Gly-Gly-Gly (SEQ ID NO:5), whereas R^2 may be Gly-Val-Leu-Gly-Gly (SEQ ID NO:11); see SEQ ID NO:17).--

Please replace the paragraph beginning at page 22, line 1, with the following:

--Similarly, w and z are independently selected and are equal to zero or one within the above formula for the ADNF III polypeptide. The term independently selected is used herein to indicate that w and z may be identical or different. For example, w and z may both be zero or, alternatively, w and z may both be one. In addition, w may be zero and z may be one or, alternatively, w may be one and z may be zero. Moreover, if w and z are both one, the amino acid sequences R^3 and R^4 may be the same or different. As such, the amino acid sequences R^3 and R^4 are independently selected. If R^3 and R^4 are the same, they are identical in terms of both

chain length and amino acid composition. For example, both R^3 and R^4 may be Leu-Gly-Leu-Gly-Gly (SEQ ID NO:7); see SEQ ID NO:18. If R^3 and R^4 are different, they can differ from one another in terms of chain length and/or amino acid composition and/or order of amino acids in the amino acids sequences. For example, R^3 may be Leu-Gly-Leu-Gly-Gly (SEQ ID NO:7), whereas R^4 may be Leu-Gly-Leu-Gly (SEQ ID NO:12); see SEQ ID NO:19. Alternatively, R^3 may be Leu-Gly-Leu-Gly-Gly (SEQ ID NO:7), whereas R^4 may be Leu-Gly-Leu-Gly-Leu (SEQ ID NO:13); see SEQ ID NO:20.--

Please replace the paragraph beginning at page 22, line 15, with the following:

--Within the scope, certain ADNF I and ADNF III polypeptides are preferred, namely those in which x, y, w, and z are all zero (*i.e.*, SALLRSIPA (SEQ ID NO:1) and NAPVSIPQ (SEQ ID NO:2), respectively). Equally preferred are ADNF I polypeptides in which x is one; R^1 is Val-Leu-Gly-Gly-Gly (SEQ ID NO:5); and y is zero; see SEQ ID NO:21. Also equally preferred are ADNF I polypeptides in which x is one; R^1 is Val-Glu-Glu-Gly-Ile-Val-Leu-Gly-Gly-Gly (SEQ ID NO:6); and y is zero; see SEQ ID NO:22. Also equally preferred are ADNF III polypeptides in which w is one; R^3 is Gly-Gly; and z is zero; see SEQ ID NO:23. Also equally preferred are ADNF III polypeptides in which w is one; R^3 is Leu-Gly-Gly; z is one; and R^4 is Gln-Ser; see SEQ ID NO:24. Also equally preferred are ADNF III polypeptides in which w is one; R^3 is Leu-Gly-Leu-Gly-Gly- (SEQ ID NO:7); z is one; and R^4 is Gln-Ser; see SEQ ID NO:25. Also equally preferred are ADNF III polypeptides in which w is one; R^3 is Ser-Val-Arg-Leu-Gly-Leu-Gly-Gly (SEQ ID NO:8); z is one; and R^4 is Gln-Ser; see SEQ ID NO:26. Additional amino acids can be added to both the N-terminus and the C-terminus of these active sites (SALLRSIPA (SEQ ID NO:1) or NAPVSIPQ (SEQ ID NO:2)) without loss of biological activity as evidenced by the fact that the intact ADNF I or ADNF III growth factors exhibit extraordinary biological activity. *See*, U.S.S.N. 08/324,297, filed October 17, 1994 (also published as WO96/11948) for the description of ADNF I polypeptides; and U.S.S.N. 60/037,404 filed February 27, 1997 and U.S.S.N. 60/059,621 filed, September 23, 1997 (also

published as WO98/35042) for the description of ADNF III polypeptides, all of which are incorporated herein by reference.--

Please replace the paragraph beginning at page 25, line 13, with the following:

--In a preferred embodiment, the ADNF I polypeptide comprises an amino acid sequence of $(R^1)_x$-Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala-$(R^2)_y$ (SEQ ID NO:3), and the ADNF III polypeptide comprises an amino acid sequence of $(R^3)_w$-Asn-Ala-Pro-Val-Ser-Ile-Pro-Gln-$(R^4)_z$ (SEQ ID NO:4). In another embodiment, x and y are both zero for the above formula for the ADNF I polypeptide (SEQ ID NO:1), and w and z are both zero for the above formula for the ADNF III polypeptide (SEQ ID NO:2). The previous discussion pertaining to R^1, R^2, R^3, R^4, x, y, and w and z, and various preferred ADNF polypeptide embodiments is fully applicable to the ADNF polypeptides used in this method of present invention and, thus, will not be repeated with respect to this particular method.--

Please replace the paragraph beginning at page 29, line 29, with the following:

--In a preferred embodiment, the pharmaceutical composition comprises ADNF polypeptide mixtures, wherein the ADNF I polypeptide comprises an amino acid sequence of $(R^1)_x$-Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala-$(R^2)_y$ (SEQ ID NO:3), and the ADNF III polypeptide comprises an amino acid sequence of $(R^3)_w$-Asn-Ala-Pro-Val-Ser-Ile-Pro-Gln-$(R^4)_z$ (SEQ ID NO:4). In another embodiment, x and y are both zero for the above formula for the ADNF I polypeptide (SEQ ID NO:1), and w and z are both zero for the above formula for the ADNF III polypeptide (SEQ ID NO:2). The previous discussion pertaining to R^1, R^2, R^3, R^4, x, y, and w and z, and various preferred ADNF polypeptide embodiments is fully applicable to the ADNF polypeptides used in this aspect of present invention and, thus, will not be repeated with respect to this aspect of the invention.--

Please replace the paragraph beginning at page 31, line 1, with the following:

--Small polypeptides including SALLRSIPA (SEQ ID NO:1) and NAPVSIPQ (SEQ ID NO:2) cross the blood brain barrier. For longer polypeptides that do not the cross blood brain barrier, methods of administering proteins to the brain are well known. For example, proteins, polypeptides, other compounds and cells can be delivered to the mammalian brain via intracerebroventricular (ICV) injection or via a cannula (*see, e.g.*, Motta & Martini, *Proc. Soc. Exp. Biol. Med.* 168:62-64 (1981); Peterson *et al., Biochem. Pharamacol.* 31:2807-2810 (1982); Rzepczynski *et al., Metab. Brain Dis*. 3:211-216 (1988); Leibowitz *et al., Brain Res. Bull.* 21:905-912 (1988); Sramka *et al., Stereotact. Funct. Neurosurg*. 58:79-83 (1992); Peng *et al., Brain Res.* 632:57-67 (1993); Chem *et al., Exp. Neurol.* 125:72-81 (1994); Nikkhah *et al., Neuroscience* 63:57-72 (1994); Anderson *et al., J. Comp. Neurol.* 357:296-317 (1995); and Brecknell & Fawcett, *Exp. Neurol.* 138:338-344 (1996)). In particular, cannulas can be used to administer neurotrophic factors to mammals (*see, e.g.*, Motta & Martini, *Proc. Soc. Exp. Biol. Med.* 168:62-64 (1981) (neurotensin); Peng *et al., Brain Res.* 632:57-67 (1993) (NGF); Anderson *et al., J. Comp. Neurol.* 357:296-317 (1995) (BDNF, NGF, neurotrophin-3).--

Please replace the paragraph beginning at page 41, line 7, with the following:

--One of skill will recognize many ways of generating alterations in a given nucleic acid sequence. Such well-known methods include site-directed mutagenesis, PCR amplification using degenerate oligonucleotides, exposure of cells containing the nucleic acid to mutagenic agents or radiation, chemical synthesis of a desired oligonucleotide (*e.g.,* in conjunction with ligation and/or cloning to generate large nucleic acids) and other well-known techniques (*see* Giliman & Smith, *Gene* 8:81-97 (1979); Roberts *et al.*, *Nature* 328:731-734 (1987)). For example, alanine scanning can be used to determine conservatively modified variants for SALLRSIPA (SEQ ID NO:1) or NAPVSIPQ (SEQ ID NO:2) (*i.e.*, by substituting

each amino acid one by one with an alanine or other small neutral amino acid and assay for activity as described herein).--

Please replace the paragraph beginning at page 49, line 10, with the following:

--These findings demonstrate that administration of ADNF polypeptides prevents alcohol-induced fetal demise, growth restrictions and learning abnormalities in a model of FAS. Adult male offspring from alcohol-treated litters were unable to learn in the Morris watermaze. However, treatment with ADNF polypeptides in addition to the alcohol prevented this learning deficit. In addition, peptide intervention was successful in the prevention of fetal death, even when given one hour after alcohol administration. Assessment of the protective effects of the peptides in the offspring demonstrated that not only were the acute effects of alcohol toxicity abated, but the long term sequelae was prevented as determined by the prevention of learning abnormalities. The remarkable *in vivo* stability of these peptides is evident as 60% of labeled NAP was recovered intact in the embryo 30 minutes after administration. Not wishing to be bound by a theory, the mechanism is likely indirect and appears to be in part linked to the embryonic growth regulator VIP, with prevention of alterations in VIP and VIP mRNA levels after alcohol administration as well as via oxidative protection. These findings suggest that ADNF polypeptides, including NAPVSIPQ (SEQ ID NO:2) and SALLRSIPA (SEQ ID NO:1), may also have therapeutic value in treatment of other conditions due to oxidative stress.--

Please cancel the present informal "SEQUENCE LISTING", page 51, and insert therefor the accompanying paper copy of the formal Sequence Listing, page numbers 1 through 8, at the end of the application.